

The amendments to the claims are fully supported by the specification as originally filed. The amendments are made to clarify the claims by correcting grammatical errors and eliminating redundancies, and are not intended to limit the scope of equivalents to which any claim element may be entitled.

Support for new claim 30 is found in originally filed claim 29. Support for new claim 31 is found in originally filed claim 23.

B. Drawings

Formal drawings, satisfying the objections raised by the Reviewing Draftsperson, will be submitted to the Patent Office upon notification of allowance of the claims.

C. Specification/Informalities

The Examiner objected to the present specification as it does not disclose the priority status. The specification has been amended to recite the priority information.

The Examiner stated that the recitation "acylxyacyl" hydrolase is not understood on page 12, line 13. The specification has been amended to recite "acyloxyacyl".

D. Non-Statutory Double Patenting Rejection

The Examiner rejected claims 22, 23, 25 and 29 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19, 20 and 22 of U.S. Patent Application No. 08/565,943. Applicants will consider filing a terminal disclaimer upon notification of otherwise allowable subject matter. A terminal disclaimer may not be appropriate once the scope of allowable claims is determined in the present application.

E. 35 U.S.C. § 112, First Paragraph Rejection

The Examiner rejected claims 22-26 and 29 under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure, because the specification does not provide evidence that the biological materials of the claimed invention are (1) known and readily available to the public; (2) reproducible from the written description, e.g., sequenced; or (3) deposited. This rejection is respectfully traversed.

On pages 12-15 of the specification (Example 1), Applicants disclose several methods of achieving a knockout mutation, that is, one which results in a lack of functional *htrB* protein as set forth in the pending claims. Applicant asserts that any of these methods can achieve a mutation in the *htrB* gene that will result in a lack of functional *htrB* enzyme and cause a phenotype characterized by endotoxin of substantially reduced toxicity. Since Applicants chose to use plasmids pB28 and pB29, however, they are willing to provide those plasmids to the public as representative embodiments. Upon receiving indication of allowable subject matter, Applicants will deposit plasmids pB28 and pB29 in compliance with the requirements set forth in *In re Lundak*, 773 F.2d 1216, 227 U.S.P.Q. 90 (Fed. Cir. 1985) and 37 C.F.R. 1.801-1.809.

E. 35 U.S.C. § 112, Second Paragraph Rejection

The Examiner rejected claims 23, 24 and 29 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention.

The Examiner states that claim 24 is indefinite in the recitation "comprising conjugation to a carrier protein"; that the use of non-idiomatic expression claim 29 is confusing; and that the term "phenol/water extraction" is not consistent with the practice in the art. Applicants have amended claims 23, 24 and 29 as suggested by the Examiner.

G. 35 U.S.C. § 102 Rejection

The Examiner rejected claims 22, 23 and 25 under 35 U.S.C. § 102(a) as being anticipated by Lee *et al.* (*J. Biol. Chem.* 270:27151-27159, November 1995).

Reconsideration of the rejection of these claims as being anticipated by Lee *et al.* is respectfully requested. As evidenced by the Declaration under 37 C.F.R. § 1.132 submitted herewith, the cited Lee *et al.* reference is not prior art, as defined by 35 U.S.C. § 102(a). It is a reference of Applicants' own work describing mutation of the *htrB* locus. This reference was published less than one year from the priority date of the present application (December 1, 1995). The court in *In re Katz* stated that the fact of co-authorship, without more, does not raise a presumption that the inventorship determination on a later-filed patent application is incorrect.

687 F.2d 450, 215 U.S.P.Q. 14 (C.C.P.A. 1982). Thus, withdrawal of this rejection is appropriate and is respectfully requested.

H. 35 U.S.C. § 103 Rejections

The Examiner rejected claims 24, 26 and 29 under 35 U.S.C. § 103(a) as being unpatentable over Lee *et al.* as applied to claim 22 above, and further in view of Gupta *et al.* (*Infect. Immun.* 60:3201-3208, 1992).

Applicant respectfully submits that the Examiner has not established the *prima facie* obviousness of the present claims. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the cited references themselves or in the knowledge generally available to an art worker, to modify the reference or to combine reference teachings so as to arrive at the claimed invention. Second, the art must provide a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim limitations. *In re Ochiai*, 37 U.S.P.Q.2d 1127 (Fed. Cir. 1997) (When evaluating the scope of a claim, every limitation in the claim must be considered.).

As discussed above, Lee *et al.* is not prior art, as defined by 35 U.S.C. §102(a). Gupta *et al.* alone does not teach or disclose all the features of the present invention. Gupta *et al.* disclose the conjugation of chemically-modified LPS to cholera toxin and other proteins. They do not, however, teach or suggest a *htrB* mutant endotoxin of substantially reduced toxicity as recited by the pending claims.

The Examiner rejected claim 29 under 35 U.S.C. § 103(a) as being unpatentable over Lee *et al.* as applied to claim 22 above, and further in view of Sprouse *et al.* (U.S. 5,641,492). Again, Lee *et al.* is not prior art, as defined by 35 U.S.C. §102(a). Sprouse *et al.* alone does not teach or disclose all the features of the present invention. Sprouse *et al.* disclose a method of making a detoxified endotoxin. Like Gupta *et al.*, however, Sprouse *et al.* do not teach or suggest a *htrB* mutant endotoxin of substantially reduced toxicity as recited by the present claims.

Applicants respectfully request that the rejections of pending claims 24, 26 and 29 under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

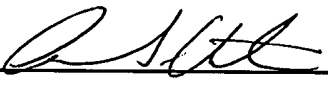
Applicant believes the claims are in condition for allowance and request reconsideration of the application and allowance of the claims. The Examiner is invited to telephone the below-signed attorney at (612) 373-6961 to discuss any questions which may remain with respect to the present application.

Respectfully submitted,

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Date 30 August 1999 By 
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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Assistant Commissioner of Patents, Washington, D.C. 20231 on August 30, 1999 (Monday).

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Name


Signature